

CLAIMS

We claim:

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1. A vector suitable for transgene delivery into mammalian cells, wherein said vector comprises a chimeric genetic construct comprising a transgene operably linked to at least two distinct posttranscriptional regulatory elements functional in cells.

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2. The vector of claim 1, wherein at least one posttranscriptional regulatory element confers increased stability to mRNAs.

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3. The vector of claim 1 or 2, wherein at least one posttranscriptional regulatory element comprises all or a portion of a UTR region of a eukaryotic mRNA.

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4. The vector of claim 3, wherein said UTR region is selected from tau 3'UTR, TH3'UTR and/or APP5'UTR or a functional portion thereof.

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5. The vector of claim 1 to 4, wherein at least one posttranscriptional regulatory element comprises all or a functional portion of a WPRE element.

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6. A vector suitable for transgene delivery into mammalian cells, wherein said vector comprises a chimeric genetic construct comprising a transgene operably linked to a WPRE element and to an APP5'UTR region.

7. A vector suitable for transgene delivery into mammalian cells, wherein said vector comprises a chimeric genetic construct

comprising a transgene operably linked to a WPRE element, an APP5'UTR region and a tau3'UTR region.

5 8. A vector suitable for transgene delivery into mammalian cells, wherein said vector comprises a chimeric genetic construct comprising a transgene operably linked to a WPRE element, an APP5'UTR region, a tau3'UTR region and a TH3'UTR region.

10 9. The vector of any one of claims 5 to 8, wherein said WPRE element comprises all or a functional fragment of SEQ ID NO: 1.

10. The vector of any one of claims 4 to 8, wherein said APP5'UTR region comprises all or a functional fragment of SEQ ID NO: 2.

15 11. The vector of any one of claims 4, 7 or 8, wherein said tau3'UTR region comprises all or a functional fragment of SEQ ID NO: 3.

12. The vector of claims 4 or 8, wherein said TH3'UTR region comprises all or a functional fragment of SEQ ID NO: 4.

20 13. The vector of any one of the preceding claims, wherein said vector further comprises a promoter controlling transcription of the transgene in said mammalian cells.

25 14. The vector of any one of the preceding claims, wherein said vector further comprises a marker gene.

30 15. The vector of any one of the preceding claims, wherein said vector further comprises a polyadenylation signal operably linked to said transgene.

16. The vector of any one of the preceding claims, wherein said vector is selected from a plasmid and a recombinant virus.

5 17. The vector of claim 16, wherein said vector is a replication-defective adenovirus, a replication-defective adeno-associated virus or a replication-defective retrovirus, including replication-defective lentiviruses.

10 18. The vector of any one of the preceding claims, wherein the transgene is selected from a transgene coding for a growth factor, a neurotrophic factor, a cytokine, a ligand, a receptor, an immunoglobulin and an enzyme.

15 19. A recombinant cell comprising a chimeric genetic construct as described in anyone of claims 1 to 18 or a vector of claims 1 to 18.

20. Use of a vector of anyone of claims 1 to 18 or a recombinant cell of claim 19 for the manufacture of a medicament to treat a disease.

20 21. A composition comprising a chimeric genetic construct as described in anyone of claims 1 to 18, a vector of anyone of claims 1 to 18 or a recombinant cell of claim 19 and a pharmaceutically acceptable excipient or carrier.

25 22. The composition of claim 21 for treating a human disease.

30 23. The use of claim 20 or the composition of claim 22, wherein said human disease is a neurodegenerative disease preferably selected from Parkinson disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), Huntington's disease and retinal degenerative diseases.

24. A method of expressing a transgene in a mammalian cell *in vitro* or *ex vivo*, the method comprising:

- a. providing a chimeric genetic construct comprising said transgene operably linked to at least two distinct posttranscriptional regulatory elements, and
- b. introducing said construct into mammalian cells, said introduction causing expression of said transgene in said mammalian cells.

25. The method of claim 24, comprising:

- a. providing a vector according to any one of claims 1-18, and
- b. introducing said vector into mammalian cells, said introduction causing expression of said transgene in said mammalian cells.

26. The method of claims 24 to 25, wherein said mammalian cells are neural cells preferably selected from glial and neuronal cells.

27. The method of claims 24 to 25, wherein said mammalian cells are fibroblasts.

28. The method of claim 26 or 27, wherein said mammalian cell is a human cell or a rodent cell.

29. The method of claims 24 to 27, wherein the chimeric genetic construct or vector is introduced into mammalian cells by virus-mediated infection.

30. The method of claims 24 to 27, wherein the chimeric genetic construct or vector is introduced into cells by plasmid-mediated transfection.

31. A method of expressing a transgene in glial cells, the method comprising:

- a. providing a chimeric genetic construct comprising said transgene operably linked to posttranscriptional regulatory elements comprising a WPRE element combined with a APP5'UTR or a portion thereof, and
- b. introducing said construct into glial cells, said introduction causing expression of said transgene in said glial cells.

32. A method of expressing a transgene in fibroblasts, the method comprising:

- a. providing a chimeric genetic construct comprising said transgene operably linked to posttranscriptional regulatory elements comprising a WPRE element combined with a APP5'UTR or a portion thereof, and
- b. introducing said construct into fibroblasts, said introduction causing expression of said transgene in said fibroblasts.

33. A method of expressing a transgene in neuronal cells, the method comprising:

- a. providing a chimeric genetic construct comprising said transgene operably linked to posttranscriptional regulatory elements comprising a WPRE element combined with a APP5'UTR and a tau3'UTR or a portion thereof, and
- b. introducing said construct into neuronal cells, said introduction causing expression of said transgene in said neuronal cells.

34. A method of expressing a transgene in neuronal cells, the method comprising:

- a. providing a chimeric genetic construct comprising said transgene operably linked to posttranscriptional regulatory

elements comprising a WPRE element combined with a APP5'UTR, a tau3'UTR and a TH3'UTR or a portion thereof,

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- b. Introducing said construct into neuronal cells, said introduction causing expression of said transgene in said neuronal cells.